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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,497	02/24/2004	Mark W. Becker	375551-001C2	9922

37509 7590 05/03/2006

DECHERT LLP
P.O. BOX 10004
PALO ALTO, CA 94303

EXAMINER	
MARTIN, PAUL C	

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,497	BECKER ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending in this application and were examined on their merits.

Information Disclosure Statement

The information disclosure statement filed 07/19/04 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Copies of the foreign patents and all of the cited non-patent literature have not been received and scanned as of the filing of the latest IDS, which was filed 07/19/04.

Specification

The use of the trademarks Chiralpak and Zorbax has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 4 and 5 are objected to because of the following informalities: The first use of the acronyms HIV, HBV, PMPA and PMEA should be followed by an explanation for the abbreviation. Appropriate correction is required.

Claim 12 is objected to because of the following informalities: Claim 12 contains the phrase "The method of Claim 12...". Perhaps the Applicant meant for the second 12 to be an 11? Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the limitation "amidate" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9 and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Glazier *et al.* (5,627,165).

Glazier teaches a method of screening for antiviral activity of PMEA [9-(2-phosphonylmethoxyethyl)adenine] prodrugs on HIV infected human T-lymphocyte (lymphatic tissue) (CEMss) and HBV infected hepatocytes (liver tissue) and by administering the prodrug to a target tissue (HIV/HBV infected) and a non-target (uninfected) control; and determining the antiviral activity conferred by the prodrug on the tissues and selecting a prodrug having an activity in the infected tissue greater than 10 times that if the non-infected tissue. (Column 36, Lines 35-48 and Column 37, Lines 5-22 and Columns 38 and 39, Tables).

Glazier teaches the administration of prodrugs to mice in order to determine the antiviral activity (Column 39, Lines 40-59).

Glazier teaches wherein certain prodrugs are known to be toxic for TDT+ leukemia cells (Column 27, Lines 34-35).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glazier *et al.* (5,627,165) in view of Starrett *et al.* (5,663,159).

The teachings of Glazier were discussed above.

Glazier does not teach wherein the prodrug is a phosphonoester, phosphonoamidate or mixed phosphonoester/phosphonoamidate or wherein the the ester is an aryl ester or the amidate is an amino acid amidate.

Glazier does not teach wherein the target and non-target tissues are in an animal, or wherein the activity in the target and non-target tissues is determined by assaying the amount of at least one metabolite of the prodrug.

Glazier does not teach wherein the metabolite is either the parental drug or the diphosphate of the parental drug.

Glazier does not teach wherein the target tissue is hematological and the activity is anti-tumor or wherein the tissue is malignant and the non-target tissue is the same tissue but non-malignant.

Starrett teaches wherein the PMEA prodrug is an aryl ester phosphonoester (Columns 11 and 12, Table 1, Fig. 1, Examples 3, 34 and 35) and wherein the PMEA prodrug is a phosphonoamidate (Columns 11 and 12, Table 1, Fig. 1, Example 26). For purposes of examination, it is deemed by the Examiner that claim 6 limits claim 5 to the prodrugs a) phosphonoamidate, b) phosphonoester and c) mixed phosphonoester/phosphonoamidate and claim 7 limits claim 6 to a) amino acid amidate, b) phosphonoester and c) mixed phosphonoester/phosphonoamidate that teachings meeting the limitations of claim 8 will by default meet the limitations of claim 7.

Starrett teaches administration of a prodrug to rats and assaying the amount of metabolite of the parental prodrug PMEA that is bioavailable based on urine excretion data (Column 9, Lines 59-67 and Column 10, Tables).

Starrett teaches wherein PMEA was found to have anti-tumor activity against intraperitoneal P388 leukemia (Column 2, Lines 40-41).

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Glazier for determining the activity of a prodrug in target and non-target tissues with those of Starrett for determining the amount of metabolite of the prodrug in the target and non-target tissues as a means of confirming that the effect or activity seen in the cell death and toxicity assays of Glazier were in fact due to concentrations of metabolically processed and bioavailable prodrug in the target tissues rather than just in urine as taught by Starrett. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the method of Glazier in live animal models as a way of further demonstrating the potential applicability of a prodrug in treatment in a more complex system than tissue culture. One of ordinary skill in the art would have recognized that as both references disclose the use of anti-tumor prodrugs in treating the hematological, tumor causing disease of leukemia, that the method of Glazier could be easily adapted to using malignant tissue and non-malignant tissue instead of virally infected tissue and non-infected tissue. One of ordinary skill in the art would have recognized that the metabolite could be in alternate forms depending on the prodrug used and the diphosphate of the parental drug would be an obvious variant of a parental drug such as PMEA. One of ordinary skill in the art would have recognized that it would have been obvious to use variants of PMEA prodrugs as taught by Starrett in the method of Glazier in order to achieve the best possible results for anti-viral activity.

One of ordinary skill in the art would have been motivated to make these changes in order to obtain more data which could be used to assess the effects of administering prodrugs on more complex living systems, for a variety of diseases, in different tissues. There would have been a reasonable expectation of success in adapting the method of Glazier and combining the methods of Glazier and Starrett due to the overlap in scope of the two methods in characterizing the effects of similar prodrugs on living systems.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one with ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence or evidence to the contrary.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Martin
Examiner
Art Unit 1655

04/17/06

Patricia Leith
Primary 1655